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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/447,681 | 11/23/1999 | JACK A. ROTH | INRP.003--2/ | 4103 |

7590 03/17/2005

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| EXAMINER | |
|---|---|
| CROUCH, DEBORAH | |
| **ART UNIT** | **PAPER NUMBER** |
| 1632 | |

DATE MAILED: 03/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/447,681 | ROTH, JACK A. | |
| | Examiner | Art Unit | |
| | Deborah Crouch, Ph.D. | 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *13 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *67 and 86-89* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *67 and 86-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 November 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant's arguments filed December 13. 2004 have been fully considered but are not persuasive. The amendment has been entered. Claims 67 and 86-89 are pending.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 67 and 86 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 22 and 37 of copending Application No. 08/626,678 for reasons presented in the office action mailed June 10, 2004.

The present claims are to pharmaceutical compositions comprising adenoviral vectors comprising a wild-type p53 gene operably linked to a promoter (claim 86) and where the promoter is a CMV (claim 67). Claims 22 and 37 of '678 are drawn to recombinant adenovirus, which carries an adenovirus vector construct comprising an expression region encoding p53 under the control a CMV IE promoter and an adenovirus vector construct comprising an expression region encoding p53 under the control a CMV IE promoter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 67 and 86 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 5, 8-10, 12 and

15-18 of U.S. Patent No. 6,410,010 B1 for reasons presented in the office action mailed June 10, 2004.

The present claims are to pharmaceutical compositions comprising adenoviral vectors comprising a wild-type p53 gene operably linked to a promoter (claim 86) and where the promoter is a CMV (claim 67). Claims 1-3, 5, 8-10 and 15-18 of '010 are drawn to recombinant adenovirus which carries an adenovirus vector construct comprising an expression region encoding p53 under the control a CMV IE promoter.

Claims 86-89 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 12 of U.S. Patent No. 6,410,010 B1 for reasons presented in the office action mailed June 10, 2004.

The present claim is to pharmaceutical compositions comprising adenoviral vectors comprising a wild-type p53 gene operably linked to a promoter (claim 86) and where the promoter is a β-actin, SV40 or RSV (claims 87-89). Claim 12 of '010 is drawn to recombinant adenovirus, which carries an adenovirus vector construct comprising an expression region encoding p53 under the control a promoter. The pharmaceutical composition of present claims 86-89 contains the same recombinant adenovirus as encompassed in claim 12 of '010.

Claims 67 and 86 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 7 and 12 of U.S. Patent No. 6,511,847 B1 for reasons presented in the office action mailed June 10, 2004.

The present claims are to pharmaceutical compositions comprising adenoviral vectors comprising a wild-type p53 gene operably linked to a promoter (claim 86) and where the promoter is a CMV (claim 67). Claims 1, 7 and 12 of '847 are drawn to an adenovirus expression vector comprising an adenovirus expression vector comprising an ITR and a p53 gene under the control of a CMV promoter.

Claims 67 and 86 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 64 and 78 of U.S. Patent No. 6,740,320 B1 for reasons presented in the office action mailed June 10, 2004.

The present claims are to pharmaceutical compositions comprising adenoviral vectors comprising a wild-type p53 gene operably linked to a promoter (claim 86) and where the promoter is a CMV (claim 67). Claims 64 and 78 of '320 are drawn to a pharmaceutical composition comprising a recombinant adenovirus containing an adenovirus vector construct comprising an expression region encoding p53 under the control a CMV promoter and a pharmaceutically acceptable carrier, expedient or diluent.

Claims 86-89 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 77 of U.S. Patent No. 6,740,320 B1 for reasons presented in the office action mailed June 10, 2004.

The present claim is to pharmaceutical compositions comprising adenoviral vectors comprising a wild-type p53 gene operably linked to a promoter (claim 86) and where the promoter is a β-actin, SV40 or RSV (claims 87-89). Claim 77 of '320 are drawn to a pharmaceutical composition comprising a recombinant adenovirus containing an adenovirus vector construct comprising an expression region encoding p53 under the control of a promoter and a pharmaceutically acceptable carrier, expedient or diluent.

Applicant argues that the PTO, as they understand the issue, has essentially indicated that nonpharmaceutical composition claims are patentably distinct from pharmaceutical composition claims. Applicant argues that this is in contrast to the position taken by the Examiner in this application. Applicant argues that in the present prosecution, the position is taken that a pharmaceutical composition claim is similar to a composition claims. Applicant argues that previously the PTO held that nonpharmaceutical composition

claims were distinct from nonpharmaceutical composition claims. These arguments are not persuasive.

This examiner is not aware of any such directive, and has never been shown such a directive. There may have been a time when patentable distinction was made, but this should not be construed on the part of applicant that it represents a patent office policy, much less a permanent patent office policy. However, the present claims are to an adenovirus vector .... wherein the vector is comprised in a pharmaceutical composition. This makes the claim directed to a pharmaceutical composition. Therefore, in the '320 patent, the obviousness-type double patenting rejection is over present claims to a pharmaceutical composition and the pharmaceutical composition claims in '320. On the other hand, if applicant's contention is that the present claims are not to a pharmaceutical composition, then there should be no dispute of an obviousness-type double patenting conflict with application '678, and patents '010, '847 and '320. Applicant is arguing that the claims are not a pharmaceutical composition when the conflicting patent or application has claims to a pharmaceutical composition, and arguing that the present claims are to a pharmaceutical composition when the conflicting claims are to a product, which, incidentally, encompasses a pharmaceutical product. Applicant cannot argue both.

Nonetheless, the obviousness type double patenting rejections are maintained because the present claims are deemed to be to a pharmaceutical composition, which would make the pharmaceutical composition claims obvious, but which also make the product claims obvious because the product encompasses the presently claimed pharmaceutical composition.

Applicant also argues that a significant loss of patent term would be encountered as well as patent validity of issued patents and allowed claims. Applicant requests consistency in rejections.

Patent term loss and issues of validity are not reasons for overcoming what is seen as a legitimate rejection. Further, in application 08/145,826, there was a restriction between recombinant adenovirus, group I, and a method of restoring p53 function, group II. However, this application is not a parent to the present application so the argument that an obviousness type double patenting rejection cannot be made when there is a restriction was made, causing the filing of divisional applications, cannot be made. In reading applicant's response, the examiner could not find an instance where an obviousness type double patenting rejection made between a adenoviral product and a pharmaceutical composition comprising an adenoviral product was overcome because there is patentable distinction between them. All that is said is the PTO found no patentable distinction between a pharmaceutical composition and a method of treatment using the pharmaceutical composition.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 67 and 86-89 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons presented in the office actions mailed April 12, 2001, February 12, 2002, September 27, 2002, May 28, 2003, September 9, 2003 and June 10, 2004.

In summary, the present specification fails to convey that at the time of their earliest claimed priority date, October 13, 1992, that applicant's had possession of the claimed

invention. Presently amended claims are to adenoviral vectors comprising a wild-type p53 gene under the control of a promoter, wherein the vector is comprised in a pharmaceutical composition. The claims specifically, state that the promoter can be a CMV, β-actin, SV40 or RSV promoter. It is maintained that the present specification fails to provide sufficient disclosure that applicant's contemplated the claimed adenoviral vectors either figuratively or specifically. The description disclosed would not allow those of ordinary skill in the art to recognized that the presently claimed adenoviral vectors had been invented by applicant.

Applicant argues that the present specification provides adequate description of the invention, and that a person of ordinary skill would have recognized at the time of filing that applicant had possession of the claimed invention. Applicant provides citations for specification support of written description at their earliest priority date. Rebuttal for these citations appears below:

1. At page 9, lines 6-12, the specification states generally "in one specific embodiment, the invention concerns vector constructs for introducing wild type p53 genes ..."; "... wherein the wt-p3 is placed under the control of the β-actin promoter, and the unit is positioned in reverse orientation into a retroviral vector." Therefore, this citation discloses a "specific embodiment" of a vector constructs for introducing wild-type p53 into cells, and states "these embodiments involve the preparation of a gene expression unit where the wt-p53 gene is placed under the control of the β-actin promoter, and the unit is positioned in a reverse orientation into a retroviral vector." In this discussion, the only contemplation is stated to be a retroviral vector having in reverse orientation a wt-p53 gene operatively linked to a promoter. There is no contemplation of an adenoviral vector comprising a CMV promoter, or any other specifically claimed promoter, operatively linked to a wt-p53 gene at this place in the specification. Without evidence of contemplation, there is no possession at the time of filing.

2. At page 61, lines 29-30, the only vector discussed to express wild type p53 in both orientations is a retroviral vector. There is no specific disclosure of adenovirus vectors at this citation, and thus there is

no evidence provided here that appellant had possession of the claimed invention at the time of filing. Thus, this citation fails to provide the needed support for written description.

3. At page 8, line 25 to page 9, line 4, the effect which is stated to be achievable with other promoter/vector constructs, is the enhanced expression when the promoter in the retrovirus is reversed with regard to other promoters within the retrovirus (page 8, lines 25-31). This citation discusses the discovery that when the selected promoter/gene construct is aligned within the vector in an orientation that is reversed with respect to direction of transcription with respect to other promoters with in the vector, a dramatic increase in transcription of the selected gene is seen. Then the passage goes on to discuss the use of retroviral vectors where the transcription of the selected gene is in reverse orientation to other retroviral transcription. The passage continues by stating that while the increase in transcription was observed using the β-actin promoter and retroviral vector, the inventors believe that the increase will be seen other promoter/vector constructs. The examiner will agree that Appellant has contemplated in general vectors having the gene of interest operatively linked to promoter, and having both in reverse orientation for transcription relative to transcription of other genes in the vector. However, the support for other than retrovirus does not support the species of adenovirus vector comprising a CMV promoter, or any other promoter. There is no evidence provided at this citation that appellant was in possession of the claimed subject matter at the time of filing.

4. At page 14, lines 21-23, are not seen as supporting written description. A reading of the specification from at least page 5, line 7 to at least page 16, line 10, shows that this citation is embedded in a paragraph discussing antisense technology. This citation does state that "in addition to retroviruses, it is contemplated that other vectors can be employed, including adenovirus ....". However, when read in context of the paragraph, one would realize that the adenovirus contemplated contains antisense sequences. The larger relevant citation (page 14, lines 9-25) states "in broader aspects of the invention, a preferred approach will involve the preparation of retroviral vectors .....", "although the retrovirus would inhibit the growth of the tumor, the expression of the antisense construct in non-tumor cells .....", "in addition to retroviruses, it is contemplated .... adenoviruses" .As discussed above the entire paragraph, page 14, lines 9-25, contemplates only antisense. This only supports an adenoviral vector comprising an

antisense construct and not the adenovirus of the claims. Thus, this citation fails to provide evidence of possession of the claimed invention at the time of filing.

5. At page 33, lines 9-11, states more than "by way of illustration ..... mention the following vectors ... adenovirus ...". However, the paragraph begins "the particular vector which one employs for introduction of antisense intron coding sequences is not believed to be particularly crucial to the practice of the present invention... by way of illustration, but not limitation, one can mention the following vectors, including N2A,

LN, LNSX, Adenovirus and Adeno-associated virus. Thus the concept disclosed at this citation is that adenovirus can be used to introduce antisense introns.

6 and 7. At page 15, lines 1-4, and page 14, line 35 to page 15, line 2, each citation is embedded in a paragraph that begins "the particular promoter that is employed to control the expression of the antisense RNA ....". Furthermore, page 15, line 5 states that "while the β-actin promoter is preferred in the invention is by no means limited to this promoter, and one may also mention .....CMV." However, when the entire paragraph is read, "the invention" at this point is the expression of antisense sequences. Please refer to the paragraph at page 14, line 27 "the particular promoter that is employed to control the expression of the antisense RNA in a vector construct is not believed to be particularly crucial ..... where a human cell is targeted, it will be preferred to position the antisense RNA coding region adjacent to and under the control of a promoter that is capable of being expressed in a human cell ... generally speaking, such a promoter might include either a human cellular or viral promoter..... while the β-actin promoter is preferred .... CMV". Page 14, line 35 to page 15, line 2, states "generally speaking, such a promoter might include either a human cellular or viral promoter.....". However, when read in the full context, as discussed above (page 14, lines 21-23), the description is for "generally speaking" regarding promoters for use in retroviruses comprising antisense sequences, and not the claimed invention. A reading of the complete paragraph assigns the citation provided by Appellant to refer only to retrovirus vectors expressing antisense. There is no written support for the claimed invention.

8. At page 16, lines 5-10, the specification states "while the retrovirus construct aspect .... concerns the use of a β-actin promoter in reverse orientation, there is no limitation on the nature of the selected gene ..."; "thus, the invention concerns the use of antisense coding constructs as well as "sense" constructs that encode a desired proteins. The contemplation is clearly for other genes expressed in the sense or antisense orientation from the β-actin promoter in a retroviral vector. The specification at this point does not discuss adenovirus as a contemplated vector, the CMV promoter as the contemplated promoter or wt-p53 as the contemplated gene. Thus, this citation fails to provide written description of the claimed invention.

It is clear from each citation given by applicant that the contemplation in the specification is for an adenovirus comprising antisense, or retrovirus comprising a p53 gene, and not an adenoviral vector comprising a p53 gene. Further, when reading the specification as a whole there is no concept of an adenovirus comprising a p53 gene. The specification does contemplate such either clearly, literally, figuratively or even in the most remote fashion. The artisan reading the present specification would not have realized that the specification ever disclosed an adenovirus comprising a p53 gene operably linked to a promoter or a CMV promoter as part of applicant's invention.

Applicant argues that declarations by those of ordinary skill in the art have been supplied: Dr. Lou Zumstein and Dr. Philip Hands. Applicant argues that the action has not rebutted the evidence presented by these ordinary skilled artisans. Applicant argues that there is a preponderance of evidence as stated in MPEP 2163.04, and thus the rejection should be withdrawn. These arguments are not persuasive.

In previous office actions, an analysis of the specification at the citations given by declarants as evidence of written description was provided. Included was an analysis not only of the citations but also of disclosure before and after the citations. The analysis was performed as a reading of the specification and, thus, more thorough than a reading of declarant's and applicant's specific citations. The opinions of declarants Zumstein and Hands

were countered with a clear explanation. This explanation has not been rebutted. (Applicant is referred to previous office actions mailed April 12, 2001, February 12, 2002, September 27, 2002, May 28, 2003 and September 9, 2003).

Applicant argues that adenoviruses are disclosed in the specification more than in the context of antisense RNA production. Applicant argues that adenoviruses are discussed as part of the broader context of the invention disclosed on page 14, lines 9-12. Applicant argues that the following paragraph discussing promoters indeed recites particular embodiments of the invention, such as antisense. Applicant states that the specification states "generally speaking, such a promoter might include either a human cellular or viral promoter" and that the β-actin promoter is the preferred promoter but the invention is not limited to that promoter (specification, page 14, lines 35 to page 15, line 2). These arguments are not persuasive.

At each of the citations on page 14, the surrounding paragraphs are directed towards retroviral vectors and antisense expression. The disclosure of adenoviruses is within the context of substituting for retroviruses in expressing antisense. Further the context of using promoters other than the β-actin promoter is again with retrovirus expressing antisense. There is no cohesive disclosure that indicates that an adenovirus comprising a gene encoding p53 operably linked to a promoter or anyone of the claimed promoters was conveyed as an invention of applicant.

Thus, the specification fails to convey that applicant had possession of the claimed invention at the time of filing. Thus, are not entitled to the October 13, 1992 filing date. Applicant's, therefore, are entitled only to the filing date of the instant invention, November 23, 1999.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 67 and 86 remain rejected under 3 5 U. S. C. 102(b) as being anticipated by Liu et al (1994) Cancer Research 54, 3662-3667 for reasons presented in the office action mailed September 27, 2002, May 28, 2003, September 9, 2003 and June 10, 2004.

Liu teaches an adenovirus vector comprising a wild-type p53 gene operably linked to an CMV promoter (page 3662, col. 2, parag. 4).

Applicant argues the present application is entitled to the early priority date of October 13, 1992, and thus Liu does not qualify as art against the claimed invention. This argument is not persuasive.

As applicant's arguments regarding the written description rejection were not persuasive, the rejection over Liu et al is maintained.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 86-89 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al (1990) Science 250, 1576-1579 and Stratford-Perricaudet et al (1990) Human Gene Therapy 1, 241-256 in view of Wilkinson et al (1992) Nucleic Acids Res. 20, 2233-2239, Colicos et al (1991) Carcinogenesis 12, 249-255, Rajan et al (1991) J. Virol. 65, 6553-6561 and Hitt et al (1990) Virol. 179, 667-678 for reasons presented in the office mailed September 27, 2002, May 28, 2003, September 9, 2003 and June 10, 2004.

Chen et al teach retroviral vectors comprising a wild type human p53 operably linked to the retroviral LTR (page 1576, col. 3, Figure 1). Chen et al teach that wild type 53 is expressed in transduced Saos cells, and that the transduced cells failed to form colonies on soft agar or tumors in nude mice (page 1577, col. 2, line 12 to col. 3, line 8). Chen et al also teach that wild type p53 counters the transformation phenotype conferred by a mutant p53 when both genes are present in equal gene dosage (page 1579, col. 1, parag. 1 to col. 2, line 1 and col. 2, parag. 1, lines 25-28). Stratford-Perricaudet et al teach the correction of an enzyme deficiency related disorder in mice (abstract). The mice are mutant for ornithine transcarbamylase and when treated with an adenovirus vector comprising an ornithine transcarbamylase DNA sequence operably linked to the adenovirus major late promoter, the mice exhibit a reversal of the mutant phenotype (page 251, parag. 1, lines 1-3). Chen et al and Stratford Perricaudet et al do not teach adenoviral vectors comprised of a wild type p53 gene under the control of a CMV promoter, a β-actin promoter, an SV40 promoter or an RSV promoter. Wilkinson et al teach the production of an adenovirus expression system where a CMV promoter regulates expression of lacZ (page 2234, col. 1, parag. 5, lines 1-3). Wilkinson et al also teach that the adenovirus-CMV system can be used to studies of gene expression and gene regulation (page 2238, col. 2, parag. 4, lines 1-4). Colicos et al teach an adenovirus vector comprising a T4 *denV* gene operably linked to the RSV promoter, the RSV LTR (page 250, col. 1, parags. 4-7, figure 1 and figure 2). The vector, Ad5denV, was shown to partially complement the excision repair deficiency in primary fibroblasts from xeroderma pigmentosa patients (page 254, col. 1, parag. 2, and page 253, figures 6 and 7, and Table 1). Rajan et al teach an adenoviral vector comprising a cDNA sequence encoding an SV 40 small-t antigen operably linked to an SV40 promoter (page 6554, col. 1, parag. 2). Rajan et al teach that the expression of the SV40 small-t antigen results in the transactivation of adenovirus EII early promoter (page 6557, col. 1,

line 13 to col. 2, line 4). Hitt et al teach an adenovirus where the expression of the E1A gene is regulated by a human β-actin promoter (page 670, col. 1, line 12 to col. 2, line 2, and figure 1). Hitt et al teach that E1A production is 3 to 5 times higher than by wild type adenovirus (page 675, col. 2, parag. 1, lines 11-16).

Applicant argues the PTO has argued that gene therapy is an unpredictable area. Applicant argues a statement from Examiner Guzo was in a case related by priority to the present application and declaration from Deborah R. Wilson, showing that the claimed invention achieves an unexpected result in clinical efficacy. Applicant have provided a declaration from Dr. Lou Zumstein stating INGN 201 is the same Ad-p53 vector disclosed in 08/145,826. These argument are not persuasive.

The vector specifically exemplified in '826 is Ad5CMV-p53, which contains a deletion of the E1 region. Further, declarant Zumstein understands that INGN 210 is AdCMVp53 '826. "understands" is not the same as is, and thus the declaration is not persuasive. Further, '826 discloses Ad5CMV-p53, not AdCMVp53. Despite these inconsistencies, the examiner is taking Ad5CMV-p53 of the specification to be INGN 210 of the Wilson declaration. The present claims are not limited to a E1 deleted adenovirus, so the unexpected results argued are not commensurate with the scope of the present claims. While gene therapy may be unpredictable from an enablement standpoint, an art rejection is not made on the basis of unpredictability. More importantly, a showing of unexpected results to overcome an art rejection must be commensurate in scope with the claims. Thus, the Wilson declaration would only be persuasive for claims limited to the showing of unexpected results. The present claims are not so limited.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Th, 8:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deborah Crouch, Ph.D.
Primary Examiner
Art Unit 1632

March 14, 2005